DNA involved in the expression of cytokine receptor gene.

2, A diagnostic method in claim 1 wherein the cytokine receptor gene is the gene of a receptor selected from tyrosine kinase receptor family, serine-threonine kinase receptor family, interleukin receptor family, interferon receptor family, immunoglobulin receptor family, apoptotic receptor family and seven transmembrane receptor family.

3, A diagnostic method in claim 2 wherein the tyrosine kinase receptor family gene is the gene of a receptor selected form epidermal growth factor receptor, epidermal growth factor-like receptor 2 (erbB2/HER2/neu), platelet derived growth factor receptor and vascular endothelial cell growth factor receptor.

4, A diagnostic method in claim 1 wherein the cell-proliferating disease is a cell-proliferating disease selected from psoriasis, chronic rheumatoid arthritis, arteriosclerosis, restenosis, diabetic retinopathy, retinopathy of prematurity and solid tumor.

5, A diagnostic method in claim 1 wherein the specific region is a region in CpG island of promoter or intron.

6, A diagnostic method in claim 1 wherein the specific region is a region involved in the expression of epidermal growth factor receptor gene and a region represented by the nucleotide sequence from 381st position to 962nd position in the nucleotide sequence as described in Seq. ID No. 4.

7, A diagnostic method in claim 6 characterized by determining the methylation level of 668th, 671st, 687th and 697th cytosine residues in the nucleotide sequence as described in Seq. ID No. 4.

8, A diagnostic method in claim 7 characterized by analyzing the methylation level of 668th cytosine residue in the nucleotide sequence as described in Seq. ID No. 4.

9, A DNA primer having base sequence represented by Seq. ID No. 1 or 2 used for any one of diagnosis described in claims 1 to 8.

10, A diagnostic method in claim 1 wherein the specific region is the region involved in the expression of epidermal growth factor-like receptor 2 (erbB2/HER2/neu) and represented by the nucleotide sequence of Seq. ID No. 8.

11, A diagnostic method in claim 10 characterized by determining the level of methylation of 268th, 276th and 288th cytosine residues in the nucleotide sequence as described in Seq. ID No. 8.

12, A diagnostic method in claim 11 characterized by analyzing the level of methylation of 268th cytosine residue in the nucleotide sequence as described in Seq. ID No. 8.

13, A DNA primer having base sequence represented by Seq. ID No. 5 or 6 used for any one of diagnosis in claims 1 to 4 and 10 to 12.

14, A DNA having base sequence represented by Seq. ID No. 1, 2, 5 or 6.

15, A method of detecting the level of methylation of cytosine residue(s) in the specific region of DNA involved in the expression of cytokine receptor gene.

16, A method in claim 15 wherein the method of detecting the level of methylation is a method using methylation sensitive restriction enzyme, a method using chemical modification by hydrazine, permanganic acids or sodium bisulfite, an immunological method using antibodies specific to methylated DNA, affinity column chromatography method or DGGE (denaturing gradient gel electrophoresis) method.

Abstract

This invention relates to a diagnostic method for detecting cell-proliferating diseases characterized by analysis of the methylation level of cytosine residues in the region involved in the expression of cytokine receptor gene.